Exhibit C

EXPERT REPORT OF CHRISTINA PRAMUDJI, M.D.

The following is a summary of my qualifications and my opinions in this case as of the date of this report. This report is based on the information I have now. To the extent I receive additional information between now and the time of the trial, I may form additional opinions or some of my opinions may be modified.

All of my opinions are held to a reasonable degree of medical and scientific certainty and probability. Below is a summary of my general opinions as set forth in more detail in my report. All of my opinions are based on my education, training, and clinical experience, the medical literature and materials that I have reviewed, my discussions with colleagues, my research and review of the medical records and deposition testimony provided to me in this case, and from the perspective of a board-certified urologist with subspecialty board certification in Pelvic Floor Medicine and Reconstructive Surgery.

- Pelvic organ prolapse and incontinence are common conditions in women. They commonly co-occur in women. There are many risk factors for prolapse and incontinence.
- Pelvic organ prolapse and incontinence can be very distressing and burdensome to women and can cause adverse effects on women physically, mentally, and socially. Both can adversely affect quality of life and relationships.
- Pelvic organ prolapse is usually treated with a pessary, a non-surgical option, or with surgery. Conservative efforts to treat prolapse with a pessary may not

be a suitable option for some women and they may not always provide relief. Many women who try a pessary will discontinue the therapy.

- Surgery for prolapse is common, frequently involves various prolapse procedures, and is also frequently combined with other procedures such as hysterectomy and incontinence surgery.
- Pelvic floor reconstruction surgery for prolapse can be and is frequently categorized by route into the abdominal or vaginal approach, with the vaginal route most often employed. Native tissue repairs are most often done vaginally. Examples include colporrhaphy, paravaginal repair, and sacrospinous or uterosacral ligament suspensions. Surgical mesh is employed for both the abdominal (sacrocolpopexy) and vaginal approaches. The abdominal approach is more morbid and extensive, leading to higher significant complication rates, blood loss, postoperative discomfort, length of hospital stay and cost. Pelvic floor reconstruction surgery for prolapse can also be further divided by the type of prolapse, such as cystocele, rectocele, vault prolapse, or a combination of these, and as stated above multiple procedures are sometimes employed to treat site-specific defects.
- Synthetic mesh has been used to treat prolapse since the 1960s. This is because the various native tissue repairs are associated with higher rates of failure and surgeons have continually sought better options for their armamentarium. Over the past 50 years, pelvic floor surgeons have employed surgical mesh for abdominal sacrocolpopexy and for vaginal procedures, such

as the use of free cut mesh, transvaginal mesh kits or the reinforcement of colporrhaphy with mesh.

- Mesh made of monofilament, large pore polypropylene, like Gynemesh PS which is also used in the Prolift and Prosima devices and sacrocolpopexy, has been most commonly used and is the standard for both the abdominal and vaginal approaches to pelvic organ prolapse repair. The mesh is made of the same polypropylene as the Prolene suture, which can be used in vaginal vault prolapse procedures like the sacrospinous or uterosacral ligament suspension surgeries. The clinical data shows that the monofilament, large pore polypropylene like Gynemesh PS allows for adequate tissue ingrowth and is not associated with a significantly increased risk of infection over that generally associated with prolapse surgery and vaginal surgery, which is consistent with my clinical experience in hundreds of women. The data in women does not support that Gynemesh PS degrades, as reoperation rates for recurrence are low, cure rates and satisfaction is high, and complication rates are not consistent with degradation or that if it did degrade, it would have a clinically significant effect, and I have not seen evidence of mesh degradation in my clinical practice.
- Gynemesh PS has been the most studied mesh in pelvic reconstructive surgery. There are numerous randomized controlled trials and over 100 studies which demonstrate that Gynemesh PS, when used itself or in the Prolift and Prosima devices, is effective, safe and useful. No other mesh has

been studied nearly to the degree of Gynemesh PS and in this regard it surpasses all industry standards and is state of the art. It has proven efficacy and safety in both the abdominal and vaginal applications for treating POP.

- While Plaintiffs' experts posit that there are safer or better meshes like PVDF, Dynamesh, and Vypro, these meshes have not been demonstrated to be more efficacious or safer based on the reliable scientific literature nor have they been studied in the prolapse application like Gynemesh PS. As later discussed, Vypro when studied for prolapse was found to be not well tolerated. Ultrapro has been referenced as a safer alternative. However, studies of it show similar rates of mesh exposure and dyspareunia and change in sexual function as Gynemesh PS and Prolift and it has not been demonstrated to be more efficacious.
- Gynemesh PS and Prolift have a positive benefit-to-risk profile. Overall, the Gynemesh PS and Prolift provide better anatomic support than native tissue repairs and subjective satisfaction is very high, as will be discussed. Improvements in quality of life following are also frequently seen and reported in the medical literature and more recent data show improvements in quality of life that are statistically significantly higher than native tissue repair. The Prolift is minimally invasive compared to the abdominal sacrocolpopexy and less morbid.
- Prosima, which also uses Gynemesh PS, has a positive benefit-to-risk profile. Overall, the Prosima provides effective treatment of anatomic defects and

subjective satisfaction with Prosima is very high, as will be discussed. Improvements in quality of life following Prosima are frequently seen and reported in the medical literature. The Prosima is minimally invasive compared to the abdominal sacrocolpopexy and less morbid. It is also potentially less invasive than trocar based mesh kits. It is indicated for stage 2 and 3 prolapse.

- All surgeries to treat pelvic organ prolapse have risks. Like Gynemesh PS, Prolift and Prosima, other prolapse and vaginal surgeries are performed in the pelvis and utilize surgical instruments, like trocars, Stamey needles, Capio needle holders, and other needle holders, in the surgical field. Potential risks of operating in this area are well described to surgeons during training, in medical textbooks, and in the medical literature, and are well-known risks. The same is true for the tensioning of sutures, grafts, and mesh whether made of synthetic, animal or native tissue, and the potential complications such as contraction of the scar tissue or pain. Tissue contraction, pain, pelvic pain, and dyspareunia can occur with any incontinence, prolapse surgery and vaginal surgery, such as concomitant posterior colporrhaphy, native tissue vault suspensions, hysterectomy and lysis of adhesions. These risks are well known and described in the literature, as well as taught to surgeons in their education and training. The clinical data do not show a statistically significant higher risk of de novo dyspareunia, de novo pelvic or vaginal pain, or change in sexual

function, or change in vaginal length with Gynemesh PS, Prolift or Prosima compared to native tissue prolapse repair.

- Mesh exposure/erosion is the only unique risk when using Gynemesh PS and synthetic mesh, and in the case of Gynemesh PS it can be treated conservatively or easily treated in an outpatient or inpatient procedure in the majority of cases. Suture and graft erosion and other wound complications can occur with non-mesh prolapse surgeries at similar and higher rates.
- Gynemesh PS, Prolift and Prosima are not defective in its design, and from my perspective as a pelvic floor reconstructive surgeon, the devices have utility and provide a durable repair. Moreover, the risks with Gynemesh PS, Prolift and Prosima are adequately described in the IFU and professional education materials. The Patient Brochures also provides adequate information to a lay person to discuss the potential options and the device with her surgeon. It is not meant to replace the surgeon-to-patient dialogue and consenting process. The Professional Education, which is recommended and incorporated into the IFU, is industry leading and above and beyond the standard of care. Professional education discusses implantation, complications and complication management as well.

I. BACKGROUND, TRAINING AND EXPERIENCE

I am a board-certified urologist, with a subspecialty board certification of Pelvic Floor Medicine and Reconstructive Surgery. I received my M.D. degree from the University of Alabama School of Medicine in Birmingham in 1996. I then completed a general surgery and urology residency at Baylor College of Medicine in Houston, Texas, where I received extensive training in pelvic floor medicine and surgery. During this training I performed various surgeries to treat urinary incontinence and other pelvic and urologic conditions and disorders. Since then I have been in private practice for over 13 years and the focus of my practice is female urology and pelvic floor medicine.

I have vast experience with prolapse surgery having performed well over 1000 surgeries. I have used tailored Gynemesh PS as well as about 450 Prolift surgeries, 75 surgeries with Prosima, numerous other transvaginal mesh repairs for prolapse, native tissue repairs and hundreds of abdominal sacrocolpopexies including open and robotic sacrocolpopexies with mesh including Gynemesh PS. I was trained on the Prolift, Prosima, and Ethicon prolapse devices and was a proctor teaching them to surgeons across numerous states as well as at national conferences such as the AUA. I have a vast experience with mid-urethral slings, having performed over 1,000 sling procedures from various manufacturers and of various approaches. I am very familiar with the Ethicon TVT and TVT-O devices, having been trained in their use and having surgically placed them in hundreds of procedures. I have been a consultant for Ethicon and Boston Scientific in sling development. I also have extensive mesh experience in over 600 cases and have

managed mesh complications, as well. My urologic practice is dedicated solely to female urology, pelvic medicine, and reconstructive surgery. A copy of my curriculum vitae, which details my training, education and experience, is attached as **Exhibit "A"** to this report. A list of my publications is also set forth in my CV.

II. CHARGES AND TESTIMONIAL HISTORY

For my work in this case, I am charging $600 an hour for time spent reviewing and preparing. I charge $700 an hour for deposition or court testimony. In the past four years, I have given testimony as an expert in the following: Connie & Kevin Schubert v. Freeman Health System et al., Jasper County Missouri Case No. 10AO-CC00219 (8/27/2013 deposition testimony), Carolyn Lewis v. Johnson & Johnson, et al., Case No.: 2:12-cv-04301 (1/10/2014 deposition testimony), Huskey/Edwards v. Johnson & Johnson, et al., (4/11/2014 deposition testimony; Sept. 2014 trial testimony), and Bellew v. Johnson & Johnson, et al., (9/17/2014 deposition testimony).

III. MATERIALS REVIEWED

In this case, I have reviewed the medical literature, the Gynemesh PS, Prolift and Prosima IFUs, the Prolift Surgical Technique Guide, Prolift Surgeon's Resource Monograph, the devices' Patient Brochures, as well as the professional education materials including PowerPoint presentations, anatomy animations, and surgical videos used by Ethicon relating to Gynemesh PS, Prolift and Prosima. I have reviewed the

expert reports submitted by the plaintiffs and materials cited by Plaintiffs' experts. Through my training, clinical and surgical experience, professional activities including CME and conference attendance, my lecturing and professional education to other pelvic floor surgeons, and my review of the literature, I am familiar with pelvic organ prolapse, the treatment of prolapse, Gynemesh PS, Prolift, Prosima and other vaginal and abdominal prolapse surgeries, other vaginal surgeries such as hysterectomy, the use of mesh for prolapse and incontinence, the development of Gynemesh PS, Prolift, and Prosima and the safety and effectiveness of prolapse surgery including the use of Gynemesh PS, Prolift, and Prosima devices. Through these means I am also familiar with urinary incontinence, the treatment of incontinence, and the medical literature relating to incontinence, including the TVT and TVT-O devices. In preparation for my testimony, I have reviewed some of that literature, as set out in **Exhibit "B**." Exhibits that will be used to support my findings and opinions, as well as documents that I have reviewed, are identified above, cited in my report, and listed in **Exhibit "B**" as well. These materials, in addition to my personal experience, knowledge, training, and education, have informed the opinions referenced above and which follow as well.

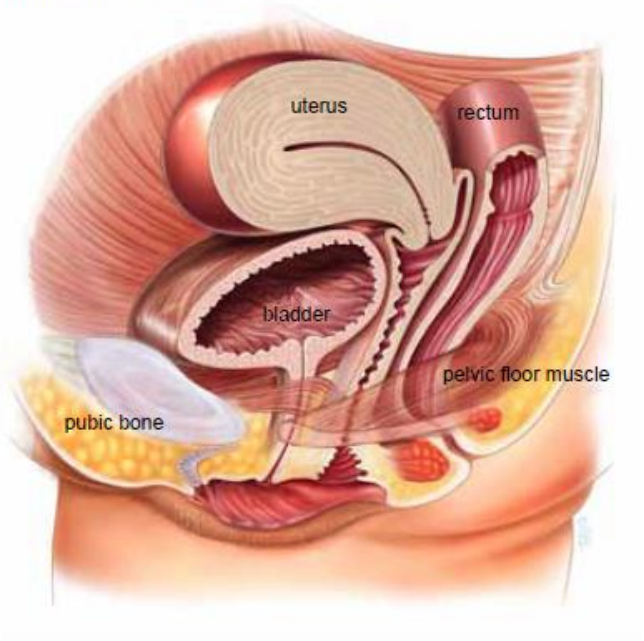
IV. OPINIONS

My conclusions and opinions are based in the practice of evidence-based medicine. As stated above, I hold all opinions set forth in this report to a reasonable degree of medical and scientific certainty and probability.

A. Pelvic Organ Prolapse - Background

Pelvic organ prolapse (POP) is the abnormal descent (dropping) of organs such as the bladder or rectum into the vagina. POP occurs due to damage and failure of the support structures in the pelvis which hold the organs in their proper anatomic position. Risk factors for POP include parity, vaginal birth, advancing age, menopause, increased body mass index (BMI) / obesity, chronic straining, smoking, chronic cough, and heavy lifting. Prior pelvic surgery such as hysterectomy also increases the risk of POP.

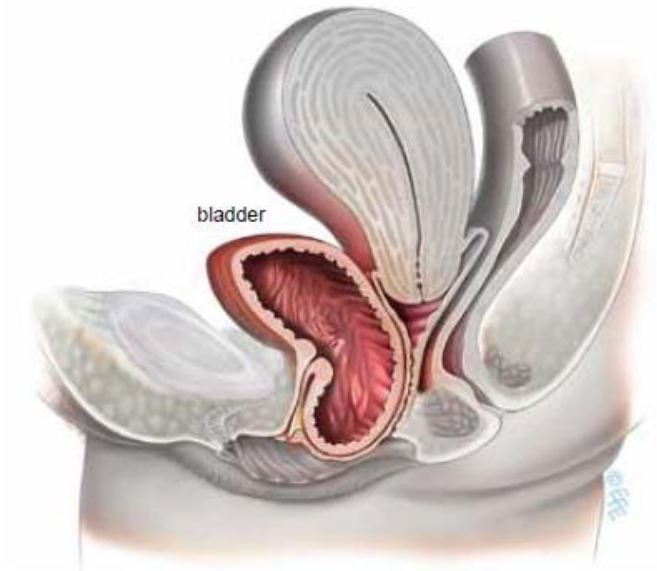
Normal anatomy, no prolapse



Prolapse of the Anterior compartment

This is the most common type of prolapse, and involves the bladder and / or urethra bulging into the vagina. Your doctor may refer to it as cystocele or cysto-urethrocele.

Anterior Compartment prolapse



IUGA 2011, Pelvic Organ Prolapse - A Guide for Women

Pelvic organ prolapse is common and is seen on examination in 40% to 60% of parous women (Maher Cochrane Database Syst. Rev. 2013). Symptoms of prolapse include a sensation of a bulge or protrusion from the vagina, heaviness, pelvic and back pain and aching, as well as symptoms of bladder, bowel or sexual dysfunction including dyspareunia. These symptoms may be directly related to the prolapsed organ, for example poor urinary stream when a cystocele is present or obstructed defecation when a rectocele is present, and they may also be independent of the prolapse, for example symptoms of overactive bladder when a cystocele is present (Maher 2013 Cochrane Review).

Cystocele, bladder prolapse, is the most common type of prolapse (Hendrix 2002 (in 16,616 women with a uterus, 34% had cystocele, 18.6% had rectocele and 14% had uterine prolapse); Fialkow 2008). In Fialkow's 10 year retrospective cohort study of 142 women, 36 recurrent cases (25%) were identified with cystocele being the most frequent element of primary (87%) and recurrent (72%) prolapse. Recurrence and reoperation are common (Clark 2003; Whiteside 2004; de Boer 2011). In the 1997 study by Olsen, 29.2% of patients had undergone at least one prior surgery for POP and/or urinary incontinence (UI) out of a group of 384 cases undergoing POP or SUI surgery (Olsen 1997). In a study of women presenting with recurrent POP symptoms, 35% of the women were found to have undergone multiple prior surgeries (Johnson 2013). In the study by Johnson, cystocele was the most common as 62% had an anterior prolapse, and 41% and 33% had posterior and apical prolapse respectively. Symptoms associated with prolapse recurrence

included 56% with incomplete emptying of bowel, 54% with urinary incontinence, 49.5% with low back pain, 42% with constipation, and 40% with dyspareunia (Johnson 2013).

B. Pelvic Organ Prolapse – Treatment

Surgery for prolapse is common, frequently involves various prolapse procedures, and is also frequently combined with other procedures such as hysterectomy and incontinence surgery. One approach to prolapse surgery is colpocleisis, an obliterative surgery. It is reserved for women who are older and/or those who do not wish to engage in vaginal intercourse.

Pelvic floor reconstruction surgery for prolapse can be and is frequently categorized by route into the abdominal or vaginal approach, with the vaginal route most often employed. Native tissue repairs are most often done vaginally. Examples include anterior and posterior colporrhaphy, paravaginal repair, and sacrospinous or uterosacral ligament suspensions. Surgical mesh is employed for both the abdominal (sacrocolpopexy) and vaginal approaches. Pelvic floor reconstruction surgery for prolapse can also be further divided by the type of prolapse, such as cystocele, rectocele, vault prolapse, or a combination of these, and as stated above multiple procedures are sometimes employed to treat site-specific defects.

Repair using native tissue for anterior colporrhaphy has high rates of recurrence, with 30–60 % failure rates (Maher 2011; Jia 2010). Jia performed a systematic review of

the efficacy and safety of mesh for anterior repair and found that mesh augmentation significantly reduced recurrence compared with traditional anterior colporrhaphy (76.9 % vs. 71.2 % cure rate, respectively).

Weber and colleagues conducted a three arm randomized controlled trial (RCT) and found significant recurrence rates -- 70% in the standard anterior colporrhaphy group failed to have satisfactory or optimal anatomic results, compared with 58% in the standard plus mesh group and 54% in the ultralateral anterior colporrhaphy group (Weber 2001). Notably, this was one of the first RCTs for a procedure that had been performed for almost 100 years. As was standard in the field, surgeons used various POP surgeries for decades relying on smaller cohort studies and their clinical experience.

Whiteside and colleagues evaluated a group of women including those in the study by Weber, undergoing prolapse and incontinence surgery and found 58% had recurrent prolapse (defined as ≥ stage II for the POPQ) (Whiteside 2004). This study is also instructive in regards to the point of follow up as only 49% of the eligible women were assessed by the authors at 1 year.

Synthetic mesh has been used to treat prolapse since the 1960s (Lane 1962). Benson and colleagues conducted one of the first RCTs comparing the abdominal sacrocolpopexy and sacrospinous ligament fixation surgery (Benson 1996). Similar to the above, these procedures had been performed for decades without “level 1” RCT support. At a mean follow up of 2.5 years, surgical effectiveness was optimal (defined as remaining asymptomatic, the vaginal apex was supported above the levator plate, and no protrusion

of any vaginal tissue beyond the hymen) in 29% of the vaginal group and 58% of the abdominal group and was unsatisfactory leading to reoperation in 33% of the vaginal group and 16% of the abdominal group (Benson 1996). Sand and colleagues conducted a RCT in 161 women who underwent anterior colporrhaphy or anterior colporrhaphy with polyglactin mesh and found a 43% failure rate in the anterior colporrhaphy group which was statistically significantly higher than the 25% in the mesh augmentation group (Sand 2001). Hiltunen and colleagues also found a statistically significant decreased risk of recurrent stage 2 or greater anterior prolapse when comparing anterior colporrhaphy reinforced with Parietene light polypropylene mesh compared to anterior colporrhaphy alone (6.7% versus 38.5%) (Hiltunen 2007).

There are risks with all surgeries. All POP and vaginal surgeries have potential risks (Diwadkar 2009; Dietz & Maher 2013). All surgical procedures to treat POP can fail. All surgical procedures have some degree of pain and discomfort. All surgical procedures to treat POP may require reoperation for failure or to treat complications. Urologists, Ob/Gyns and urogynecologists are trained on the risks of these surgeries in residency and fellowship. Mesh exposure/erosion is the only unique complication of the use of Gynemesh PS, Prolift and Prosima as compared to other POP surgeries. Moreover, many POP surgeries such as SSLF, USLS, paravaginal repair, and sacrocolpopexy rely on the use of permanent sutures, which can also lead to erosion and granulation tissue (Sokol 2012 (15% suture erosion in native tissue prolapse repair arm of Prolift RCT); Toglia 2008 (36% suture-related complications at a mean time of 18.9 months postoperatively and a 25% rate of suture removal with SSLS); Yazdany 2010 (44.6% suture related complications

including 36.1% rate of suture erosion with USLS); Svabik 2014 (15% granulation tissue rate in SSLF arm of Prolift RCT); Barber 2014 OPTIMAL trial (At 6-24 months follow up in a RCT of USLS versus SSLF, there were 19.1% granulation tissue and 15.4% suture erosion rates for the USLS arm versus 14% granulation tissue and 17.2% suture erosion rates for the SSLF arm)).

Pain, pelvic pain and dyspareunia can occur with all POP surgeries (ACOG 2011 Committee Opinion 513; AUA 2011 Position Statement on the use of vaginal mesh for the repair of pelvic organ prolapse; Lowman 2008; Francis 1961). All POP surgeries have a risk of organ damage, nerve damage, de novo SUI or urge incontinence, de novo detrusor overactivity, postoperative urinary retention, incomplete bladder emptying, abscess, infection, UTI, wound infections, bleeding, fistula, scarring and tissue contraction leading to pain, dyspareunia, vaginal shortening or vaginal tightening, and reoperation for failure or to treat complications. Sacrocolpopexy can also lead to significant hemorrhage of the sacral vessels, ileus, DVT and PE, and longer anesthesia times also lead to higher risk. Additionally recovery is longer with an abdominal incision, as well as the attendant wound complications like seroma, herniation and dehiscence. Knowledge of these risks is a basic part of female pelvic surgery training and from my standpoint as a medical doctor, these risks do not need to be incorporated into the Gynemesh PS, Prolift or Prosima IFUs.

C. Gynemesh PS / Prolift

Over the past 50 years, pelvic floor surgeons have employed surgical mesh for abdominal sacrocolpopexy and for vaginal procedures, such as the use of free cut mesh, transvaginal mesh kits or the reinforcement of colporrhaphy with mesh. This is because the various native tissue repairs are associated with higher rates of failure and surgeons have continually sought better options for their armamentarium. Over time surgeons began to explore the vaginal route of mesh repair because the abdominal approach is more morbid and extensive, leading to higher significant complication rates, blood loss, postoperative discomfort, length of hospital stay and cost.

The development of what would become Prolift followed this course. Early studies with polypropylene and Gynemesh PS showed good efficacy and an acceptable safety profile (Julian 1996; Migliari 2000; Berrocal 2004; Lucente 2004). Nicita sutured polypropylene mesh to the anterior aspect of the arcus tendineus fascia pelvis (ATFP) to treat anterior prolapse and found a 7% recurrence at two years (Nicita 1998). A case of mesh exposure and dyspareunia was treated with trimming the mesh and vaginal closure. De Tayrac and colleagues used Gynemesh tension-free with the lateral extensions of the mesh in contact with the ATFP and anchored with a transobturator approach (De Tayrac 2002). Anatomic success was 98% and mesh exposure was found in 8.3% after 18 months follow-up. The approaches and shapes of the mesh used to treat prolapse varied greatly and by surgeon. As a result, it was difficult to compare the results of one technique to the next.

In 2000, a group of French surgeons began investigating a standardized way to place a standardized shaped mesh (Berrocal 2004). Numerous studies had been done evaluating various types of mesh and routes of placement. The surgeons ultimately chose Gynemesh PS as the mesh to use for TVM because of its monofilament, large pore (Amid type 1) polypropylene properties. They chose routes to the ATFP and SSL as these had been employed previously for prolapse repair. Thus, surgeons were familiar with surgeries that targeted these areas of placement, such as the SSLF, paravaginal repair, posterior IVS, and transobturator midurethral slings. Cosson and colleagues reported on a group of 687 women implanted with TVM in a retrospective study beginning in 2002 (Cosson 2005). Intra-operative complications occurred in 1.3% consisting of hemorrhage, bladder and rectal injuries. Short-term postoperative complications occurred in 2.5%, of which 1.3% required surgical treatment. There was a rate of 0.15% for perineal cellulitis, vesicovaginal or rectovaginal fistulas. Perineal abscess occurred in 0.3%. Surgically treated granuloma formation or vaginal erosion occurred in 6.7%. The authors noted that the higher incidence reported at the beginning of the study was subsequently decreased owing to technical improvements, consisting of short incisions in the vagina and avoiding simultaneous hysterectomy. This potential increased risk was echoed in the Prolift Surgical Technique Guide which accompanied the IFU and in Professional Education materials. Surgically treated mesh shrinkages occurred in 2.8%. Recurrence occurred in 5.3% and de novo SUI occurred in 5.4%.

Prolift utilizes Gynemesh PS polypropylene mesh which is precut for the surgeon's convenience for anterior, posterior or total (anterior + posterior) repair and is combined

with a guide and cannulas. The mesh is inserted through a full thickness vaginal incision. Hydrodissection may be employed to aide in the dissection. The surgeon uses palpation when passing the guide, which is covered by the cannulas, through the ATFP or the SSL. A retrieval device is used to acquire the mesh arms and pull them through the cannulas. The mesh is placed tension free with the use of the cannulas and by pushing up and in on the vagina before removal of the cannulas.

While plaintiffs' experts opines that Prolift is dangerous because it uses "blind passage" of the guide, as noted above, surgeons use palpation when passing the guide. This method of seeing with one's hands is customary in pelvic floor surgery and is employed with other pelvic floor surgeries. For instance, surgeons cannot always see when passing sutures during a SSLF. Laparoscopy involves the "blind" use of a Veress needle during insufflation and multiple trocars are employed during a LSC. And, injury to organs and vessels occurs even during open abdominal procedures. Plaintiffs' experts also take issue with the Prolift mesh being placed transvaginally in the clean contaminated environment. However, surgeons use synthetic materials frequently in clean contaminated spaces. While the abdomen is in theory a clean environment, it can become clean contaminated during sacrocolpopexy with concomitant hysterectomy due to the open vaginal cuff or if a suture is passed through the full thickness of the vaginal wall. In any event, overall there is no increased risk of infection seen in the medical literature. Overall, the RCTs and studies show no significant difference in infection rates compared to native tissue and other prolapse and vaginal surgery. The macroporous

nature of the Gynemesh PS allows for inflammatory cell infiltration to effectively reduce the risk of infection.

Contrary to plaintiffs' experts' opinions, mesh exposure is not equivalent to infection. Mesh exposure is instead a wound complication and wound complications are seen with all prolapse surgeries whether or not they employ a graft and whether or not the graft is synthetic or biologic (Sokol 2012 - 15% suture erosion in native tissue prolapse repair arm of Prolift RCT; Toglia 2008 - 36% suture-related complications at a mean time of 18.9 months postoperatively and a 25% rate of suture removal with SSLS; Yazdany 2010 - 44.6% suture related complications including 36.1% rate of suture erosion with USLS; Svabik 2014 - 15% granulation tissue rate in SSLF arm of Prolift RCT); Barber 2014 OPTIMAL trial - At 6-24 months follow up in a RCT of USLS versus SSLF, there were 19.1% granulation tissue and 15.4% suture erosion rates for the USLS arm versus 14% granulation tissue and 17.2% suture erosion rates for the SSLF arm; Abed 2011 SGS Systematic Review - 110 studies reported on erosions with an overall rate of 10.3% (synthetic 10.3%; biological 10.1%) and 16 studies reported on wound granulation for a rate of 7.8% (synthetic 6.8%; biological 9.1 %)).

Mesh exposure can occur with vaginal placement and with sacrocolpopexy (Nygaard 2013). Suture erosion can occur with any surgery using permanent sutures. In the Iglesia/Sokol Prolift versus native tissue prolapse repair RCT, there were 5 patients with mesh exposure in the Prolift arm (15%), but there were also 5 patients in the native

tissue arm that had suture erosion (15%), and overall no mesh infection was noted (Sokol 2012).

In the RCT study by Svabik, there was mesh exposure in 8% of the Prolift cases and granulation tissue leading to vaginal blood spotting was seen in 15% of the SSLF cases (Svabik 2014). Mesh infection was not reported to occur in this study. In the study by Withagen, 14 patients (16.9%) had mesh exposure, of which 9 were asymptomatic and were treated with estrogen, while the remaining 5 patients underwent excision and the exposures resolved (Withagen 2011). Again, there were no cases of mesh infection.

In Abed's systematic review, erosion/exposure rates were 10% for synthetic and biologic grafts (range 0-29.7%) and wound granulation in 7% of synthetic grafts and 9% in biologic grafts (Abed 2011). In the study by Halaska, 16 patients (20.8%) had mesh exposure (Halaska 2012). One-quarter were noted to be symptomatic. Six patients underwent resection under general anesthesia and four with local anesthesia. Six exposures resolved with local estrogen.

Overall the data on Prolift and Gynemesh PS shows that it is more effective in anatomic correction compared to native tissue repair. Numerous RCTs support this:

Study	# Patients	Compartment	Mesh Anatomic Cure	Native Anatomic Cure	P value
Carey 2009*	139	Ant & Post	81%	65.6%	P=.07
Withagen 2011	194	All	90%	55%	p<.001
Altman 2011	389	Anterior	82%	48%	p=0.008
Sokol 2012	65	All	38%	30%	P=0.445
Halaska 2012	168	All	83.1%	60.6%	P=0.003
El Nazer 2012*	44	Anterior	80%	35%	P<0.05
Qatawneh 2013*	116	All	79%	62%	P=0.043
Svabik 2014	70	All	97%	35%	P<0.001
DaSilveira 2014	184	Anterior	86.4%	70.4%	p=0.019

*Gynemesh PS

The recent Cochrane Review echoes this conclusion specific to anterior mesh repair and found that standard anterior repair had more anterior compartment prolapse and higher awareness of prolapse than polypropylene mesh repair (Maher 2013). An earlier systematic review and meta-analysis reached similar conclusions (Jia 2008).

Other RCTs included in Table 1 of the paper by Jacquetin and colleagues show the anatomic benefit of mesh compared to native tissue:

Table 1 Randomised controlled trials comparing polypropylene mesh with traditional native vaginal tissue repairs

Reference	Total number patients	Follow up (months)	Compartment studied	Anatomic cure mesh (%)	Anatomic cure traditional (%)	*p*
Hiltunen et al. [9]	104	12	Anterior	93	62	<0.04
Sivaslioglu et al. [10]	90	12	Anterior	91	72	<0.05
Nieminen et al. [11]	105	24	Anterior	89	59	<0.05
Nguyen and Burchette [12]	75	12	Anterior	87	55	<0.05
Carey et al. [13]	139	12	Anterior Posterior	81	65.6	0.07
Nieminen et al. [14]	202	36	Anterior	87	59	<0.0001
Withagen et al. [15]	194	12	All	90	55	<0.001
Altman et al. [16]	389	12	Anterior	82	48	0.008
Sokol et al. [17]	65	12	All	38	30	0.45

(Jacquetin 2013)

Sanses and colleagues found no difference in apical success after Prolift (98.8%) compared with uterosacral ligament suspension (99.1%) or ASC (99.3%) (Sanses 2009). However, the average elevation of the vaginal apex was slightly lower. In contrast, in both RCTs by Halaska and Svabik noted above POP-Q point C was significantly higher postoperatively in the Prolift arm compared to SSLF.

The study by Altman and colleagues was a multicenter RCT in 389 patients comparing anterior Prolift to anterior colporrhaphy which had a composite primary endpoint of success that included anatomic cure (POP-Q Stage 0-I, no prolapse or anterior wall more than 1cm above the hymen) and subjective cure (lack of symptomatic vaginal bulge) (Altman 2011). The study showed a statistically significant difference in favor of Prolift for the composite endpoint – 60.8% success versus 34.5% for colporrhaphy ($p<0.001$). Of the Prolift patients, 75.4% had no symptoms of vaginal bulge compared to 62% for the colporrhaphy group ($p=0.008$ in favor of Prolift).

Similarly, a study comparing Gynemesh PS cut in the shape of a trapezoid to anterior colporrhaphy showed significantly better anatomic improvement for the

Gynemesh PS arm at 24 months follow up -- POP-Q was optimal in 80% with Gynemesh PS compared to only 35% in the anterior colporrhaphy arm ($p<0.05$) and points Aa and Ba were significantly improved with Gynemesh PS compared to native tissue ($p<0.01$). (El-Nazer 2012) Subjective symptom improvements were seen with Gynemesh PS and colporrhaphy for urinary incontinence or urgency, voiding difficulty, vaginal pressure/bulge and sexual dysfunction symptoms. However, symptom improvement was significantly better ($p<0.05$) with Gynemesh PS for voiding difficulty and vaginal bulge; thus, a better functional outcome was achieved in the mesh group. The authors commented that this would reflect its beneficial effect on the patient satisfaction due to better quality of life.

Another study comparing Gynemesh PS to native tissue repair in patients with Stage 3-4 uterovaginal prolapse showed a lower rate of repeat surgery for recurrent pelvic organ prolapse with Gynemesh PS ($p=0.03$) and a high rate 89% of subjective success. Additionally, a recent study showed statistically significant higher anatomic cure as well as patient Quality of Life (QoL) improvements for Total Prolift versus native tissue apical repair. (daSilveira 2014)

Consistent with these benefits seen, the other RCTs also show improvement in subjective cure assessments and improvements in quality of life following Prolift:

- A high level of satisfaction with surgery (91.5%) and improvements in symptoms and quality-of-life data were observed at 12 months compared to baseline (Carey 2009).
- Subjective improvement was seen in 81% of patients. At 12 months, significant improvements in the Urogenital Distress Inventory domains "genital prolapse," "pain" and "overactive bladder," and "physical functioning" of the Incontinence Impact Questionnaire were noted. Defecatory Distress Inventory domains "pain" and "incontinence" scored significantly better in the Prolift group compared with the conventional group at 12 months ($p=0.01$ and $p=0.05$ respectively) (Withagen 2011).
- Quality of life improved and 96.2% of patients reported a cure of bulge symptoms (Sokol 2012).
- Significant improvement was observed in the Urinary Impact Questionnaire (UIQ), the Colorectoanal Impact Questionnaire (CRAIQ), and the Pelvic Organs Prolapse Impact Questionnaire (POPIQ) scoring and there was less improvement of bowel symptoms (CRAIQ) in the SSLF group than in the Prolift group (Halaska 2012, table 3).
- Significantly better functional symptom improvements were seen with Gynemesh PS for voiding difficulty and vaginal pressure/bulge versus anterior colporrhaphy. Significant improvement was also seen for

symptoms of urinary incontinence or urgency and sexual dysfunction symptoms. (El-Nazer 2012, table 4)

- Improvements from baseline were seen in the scores for POPDI (Pelvic Organ Prolapse Distress Inventory), UDI (Urinary Distress Inventory) and CRADI (Colorectal Distress Inventory) questionnaires. (Svabik 2014)
- In addition to significantly better anatomic improvement, subjective outcomes as assessed by the Prolapse Quality-of-Life Questionnaire (PQoL) were significantly better for Prolift compared to native tissue prolapse repair at 1-year follow-up (DaSilveira 2014, table 5).

These studies also show low rates of reoperation for prolapse recurrence. Longer term studies with Prosima, Prolift and Gynemesh PS in the TVM studies, which utilized the same shape of mesh as Prolift and the same routes of placement, have also shown a low rate of reoperation for prolapse, good efficacy and subjective cure / quality of life improvements, and acceptable rates of complications.

Benbouzid studied Prolift in a cohort of patients with 4.5 years follow up and found no recurrence leading to reoperation and an 85% cure rate defined as POP-Q Stage 0-1 (Benbouzid 2012). No recurrences were beyond POP-Q Stage II. Mesh exposure occurred in four patients (5.3%), with two undergoing revision and two successfully treated with estrogen. The authors noted that a low mesh exposure rate was also reported after a median follow up of 38 months by de Landsheere and colleagues, which is further discussed below.

Table 5 provides additional Prolift studies for comparison and they show good efficacy rates and acceptable rates of mesh exposure, which can often be treated conservatively:

Table 5 Results of Prolift surgery according to the previous literature

Series (reference)	No. patients	Device	Type	Mean follow up	Cure rate (anatomical)	Mesh exposure	Study design
Present series	75	Prolift	Anterior: 51 Posterior: 3 Total: 20	54 months	81.5%	5.3%	Retrospective
de Landsheere 2011[14]	526	Prolift	Anterior: 48 Posterior: 103 Total: 373	38 months†	N/A	3.6%	Retrospective
Vaiyapuri 2011[16]	254	Prolift	Anterior: 106 Posterior: 20 Total: 128	12 months	95.6%	11.5%	Retrospective
Milani 2011[17]	127	Prolift+M	Anterior: 41 Posterior: 16 Total: 70	12 months	77.4%	10.2%	Prospective
Huang 2011[13]	65	Prolift	Total: 65	24.5 months†	94%	2%	Retrospective
Wetta 2009[18]	50	Prolift	Anterior: 16 Posterior: 16 Total: 18	14 months	98%	2%	Prospective
Van Raalte 2010[19]	91	Prolift	Anterior: 46 Posterior: 28 Total: 23	19 months†	86.6%	0%	Prospective
Nair 2011[20]	60	Prolift	Anterior: 21 Posterior: 12 Total: 27	29 months	85%	15%	Prospective
Elmer 2009[21]	252	Prolift	Anterior: 121 Posterior: 68 Total: 63	12 months	80%	11%	Prospective
Hollander 2010[23]	323	Prolift	Anterior: 88 Posterior: 91 Total: 144	20 months	87%	11.5%	Retrospective

†Median follow up.

Also, as a comparison, Benbouzid observed that the long-term studies published about sacrocolpopexy reported significant mesh exposure between 6 and 9% (Ross JW & Preston M. Laparoscopic sacrocolpopexy for severe vaginal vault prolapse: five-year outcome. J. Minim. Invasive Gynecol. 2005; 12:221–6; Higgs PJ, et al. Long term review of laparoscopic sacrocolpopexy. BJOG 2005; 112:1134–8).

More recently, Nygaard and colleagues published the longer term results of the NIH funded extended CARE study involving abdominal sacrocolpopexy (Nygaard 2013). Of the 322 patients enrolled in the CARE trial, 215 were available for enrollment in extended CARE and 126 (only 39% of the original cohort) were available for evaluation at 7 years after their surgery. Of these 126 women, 90 were available for both physical examination and quality-of-life interviews and the remaining women had quality-of-life telephone interviews only. The probability of mesh erosion at 6.2 years was 10.5%. Of the 23 women with mesh erosions, 15 underwent excision in the operating room (13 via the vaginal route and 2 via the abdominal route), 4 were given estrogen cream, and 4 were asymptomatic. An updated composite endpoint of failure including anatomic and subjective measures was utilized and showed failure in 48% of the patients undergoing ASC + Burch and 34% without Burch. POP-Q values had to be adjudicated in 57 instances upon discovery of several discrepant values. 5% of the study population available to be assessed had undergone surgical retreatment for prolapse recurrence. This study again highlights the difficulty in following patients in clinical studies over extended periods of time.

de Landsheere and colleagues reported on reoperation rates for a large cohort of 524 patients who had undergone Prolift with a mean follow up of 38 months. (de Landsheere 2012). Rate of reoperation for mesh-related complications was 3.6% (which included 2.5% for mesh exposure, 0.2% for mesh infection, and 0.4% for severe symptomatic mesh retraction) and prolapse recurrence was 3%. This rate of surgery for mesh exposure is comparable to the 3.2% seen in the RCT by Altman (Altman 2011).

Jacquetin and colleagues reported on the French TVM study for which 91% of the patients were available at the five year follow up (Jacquetin 2013). By five years, only 4 patients (5%) required reoperation for prolapse recurrence. Anatomic success defined as POP-Q Stage 0-1 was 79% at 5 years. When using a composite outcome (like that employed by Nygaard in the extended CARE trial discussed above) with success defined as leading edge above the hymen (<0), no bulge symptoms and no reintervention for prolapse, the success rate was 84% at 5 years. Quality of life improvements were statistically significant and were sustained. Fourteen patients (16%) had mesh exposure with 8 resections, the majority of them occurring in the first year and none were symptomatic at 5 years. De novo dyspareunia was reported by 10% of the patients but none at the 5 year interval. This rate is in line with or lower than dyspareunia rates seen with other prolapse surgeries as further discussed below. The rate of pelvic pain at 5 years was very low and decreased compared to baseline.

Miller and colleagues reported on the US TVM study for which 78% of the patients (66/85) were available at the five year follow up (Miller 2011). By five years, only 5 patients (7.6%) required reoperation for prolapse recurrence with only 2 (3%) of these patients in the treated compartment. Overall anatomic success rate defined as POP-Q Stage 0-1 was 67% and anatomic success rates in the treated compartments was 77% at 5 years. When defined as treated side leading edge above the hymen, success rates were 89% at 5 years. Statistically significant improvements in quality-of-life and Prolapse-Specific Inventory scores were sustained over 5 years. Mesh exposure was observed in 16 of 85 patients (19%) over the 5 years and 9 required partial mesh excision. There were 3

patients with some degree of dyspareunia reported between 3 and 5 years, whereas in more patients, 8 in total, preexisting dyspareunia resolved. Representing a positive net effect on dyspareunia. Moreover, pain also improved and decreased from baseline. And, overall there was an improvement in sexual function. After a 5-year period, only 1 case of de novo dyspareunia was observed in those patients sexually active before surgery, whereas resolution of this complaint was noted in at least 8 of 12 patients with preexistent dyspareunia.

Similar results were observed by Lowman and colleagues who evaluated 129 patients undergoing Prolift (Lowman 2008). At baseline, 36.8% of sexually active women reported dyspareunia. This is a significant proportion of women with dyspareunia before surgery, but is consistent with the medical literature. The rate of de novo dyspareunia was lower than or comparable to rates with other prolapse repairs:

TABLE 4
De novo dyspareunia after prolapse surgery

Dyspareunia	ASC N = 224 (148)[a] Handa et al[21]	SSLF N = 287 (106)[a] Maher et al[6]	USS N = 110 (34)[a] Silva et al[27]	APR N = 165 (81)[a] Weber et al[18]	Prolift N = 129 (57)[a]
Baseline (preop) dyspareunia (%)	40.5 (60/148)	Unknown	20.6 (7/34)	8.0 (6/81)	36.8 (21/57)
De novo (postop) dyspareunia (%)	14.5 (11/76)	36.1 (22/61)	25.9 (7/27)	19.0 (14/75)	16.7 (6/36)

[a] Number sexually active preop.

Lowman. Does the Prolift system cause dyspareunia? Am J Obstet Gynecol 2008.

As can be seen, the rate of de novo dyspareunia ranged between 14.5% and 36.1%. Compared to the 16.7% (n=6) de novo dyspareunia rate, 33% (n=7) of the 21 women with dyspareunia at baseline had resolution. The authors reported that 92% of those with novo dyspareunia described insertional dyspareunia or dyspareunia

throughout the act of intercourse which may be attributed to perineorrhaphy as it was reportedly routinely performed in Lowman's practice. The authors also note that alternatively the dyspareunia may be due to levator myalgia, although the numbers suggest otherwise as this was only diagnosed in 11% of patients and in any event is a treatable condition. I agree with Lowman that dyspareunia is commonly reported in reproductive-aged women, menopausal women, and especially in women with pelvic floor disorders. For example, Sobhgol and colleagues performed a cross-sectional survey of 319 women aged 15-49 years and found that 54.5% reported dyspareunia (Sobhgol 2007). This is in agreement with Dietz and Maher who observed that up to 64 % of sexually active women attending a urogynecology clinic suffer from female sexual dysfunction (Dietz & Maher 2013).

Dietz and Maher reviewed the impact of pelvic organ prolapse surgery on sexual function in connection with the 5th International Collaboration on Incontinence and found that the use of mesh is associated with neither a worsening in sexual function nor an increase in de novo dyspareunia compared with non-mesh native tissue repair:

Table 1 Meta-analysis sexual function data from randomised controlled trials (RCT) comparing transvaginal mesh with native tissue repairs

Reference	De novo dyspareunia		Postoperative dyspareunia		Postoperative PISQ score	
	Vaginal mesh	Native tissue	Mesh	Native tissue	Mesh	Native tissue
Altman et al. [15]			8/110	2/101	33.1±6.7 35.1 (1.4)	32.2±7.2 35.0 (1.4)
Vollebregt et al. [11]	3/20	2/21				
Carey et al. [12]	5/18	5/12	12/30	13/33	Change −6.9	Change −7.8
Sivaslioglu et al. [14]	2/43	0/42				
Nguyen and Burchette [13]	2/22	4/26	2/23	2/23	33±3 34±6	32±4 33±3
Iglesia et al. [21]	1/11	3/14			31/34	32/35
Milani et al. [17]	3/37	3/29	9/53	12/51	35±5.7 34.0±6.7	31.5±7.2 34.7±5.7
Total	16/151 (10.6 %)	17/144 (11.8 %)	31/216 (14.4 %)	26/207 (12.5 %)	0.09 (−0.17, 0.36) No difference	

An evaluation of the earlier noted RCTs between Gynemesh PS and Prolift and native tissue repair showed no overall difference in de novo dyspareunia, de novo pelvic pain, de novo pain, sexual functioning by PISQ scores, change in total vaginal length and change in vaginal caliber (Carey 2007; Withagen 2011; Altman 2011; Sokol 2012; Halaska 2012; El-Nazer 2012; Svabik 2014; daSilveira 2014).

For example, in the study by Carey, there was no difference in de novo dyspareunia following surgery (Carey 2009). Dyspareunia following surgery was considered to be because of vaginal stenosis in three women in the mesh group and five women in the no mesh group. Two women underwent vaginoplasty for vaginal stenosis and both were from the no mesh group.

In the study by Sokol and Iglesia, no statistically significant differences were found between Prolift (9.1%) and the no-mesh group (21.4%) with respect to new-onset dyspareunia (p=0.60, table 4), and sexual function based on PISQ-12 improved significantly and was not different between the groups (Sokol 2012). In the study by El-Nazer, baseline rates of dyspareunia were 41.1% for Gynemesh PS and 44.4% for anterior colporrhaphy. Both groups had a majority of patients with improvement and there was no de novo dyspareunia with Gynemesh PS while the anterior colporrhaphy group had 8.3% de novo dyspareunia. (El-Nazer 2012) Overall the rates of sexual function, dyspareunia and change in total vaginal length were similar. In another recent study, dyspareunia rates at 12 months were lower for Prolift compared to native tissue prolapse repair and nonsignificant. (DaSilveira 2014)

Thus, the mesh is not the cause of dyspareunia as similar rates are seen with procedures utilizing no mesh. Instead dyspareunia is attributable to numerous things such as vaginal surgery and prolapse surgery itself, vaginal atrophy, wound healing, muscle spasms and tenderness/myalgia, partner issues, decreased estrogen and other factors. These are all well known by pelvic floor surgeons. Although plaintiffs' experts point to mesh contraction as a supposed cause of dyspareunia, this is incorrect. The mesh does not contract. Instead, during wound healing the tissues contract whether or not mesh is present. Given that there is no difference in total vaginal length or caliber compared to native tissue, contraction if it does occur is no different than that seen with native tissue.

The RCTs also do not show a significant difference in pelvic and genital pain. In the study by Withagen, pelvic pain decreased compared with baseline, and at 12 months, de novo pelvic pain was reported by 2/50 (4%) in the no mesh group and 4/53 (7.5%) in the Prolift group (p=0.44, table 3) (Withagen 2011). Also of note, dyspareunia decreased at 12 months compared with baseline, and at 12 months, de novo dyspareunia was reported by 3/29 (10%) in the no mesh group and 3/37 (8%) in the Prolift group (p=0.75, Table 3).

In the study by Halaska, no statistically significant difference in pelvic pain was seen between Prolift and SSLF (Halaska 2012, table 2). Additionally there was no difference in dyspareunia. In the study by Altman, no difference in pelvic or genital pain was observed (Altman 2011, table 4). Additionally, PISQ-12 scores modestly improved.

There was no significant difference in pain during sexual intercourse reported to occur usually or always (2% in the no mesh group and 7.3% Prolift (p=0.07)). 40% of the no-mesh group and 48% of the mesh-repair group answered that they were "usually" or "always" satisfied with their sexual relationships with their partners (p=0.37). In another recent study, post-operative pain rates were similar, and at 12 months the rate of pain was lower for Prolift compared to native tissue prolapse repair (8.6% versus 2.3%). (DaSilveira 2014)

Overall, these data show that Gynemesh PS and Prolift are safe and effective and biocompatable. While Plaintiffs' experts posit that there are safer or better meshes like PVDF, Dynamesh, and Vypro, these meshes have not been demonstrated to be more efficacious or safer based on the reliable scientific literature nor have they been studied in the prolapse application like Gynemesh PS. Vypro when studied for prolapse was found to be not well tolerated by the TVM Group. (Jacquetin 2004 ICS) Ultrapro has been referenced as a safer alternative. However, studies of it show similar rates of mesh exposure and dyspareunia and change in sexual function as Gynemesh PS and Prolift and it has not been demonstrated to be more efficacious. (Milani 2012; Bhatia 2012; Quenemer 2014).

While the most recent Cochrane Review acknowledges with permanent polypropylene mesh like Gynemesh PS, there are lower rates of awareness of prolapse, reoperation for prolapse, and prolapse on examination than native tissue repair, with no difference in repeat surgery for incontinence and no difference in dyspareunia versus

native tissue, the absorbable meshes like Vypro and Ultrapro have not demonstrated similar results (Maher 2016 Cochrane Review).

Additionally, Plaintiff's experts' claims that the mesh is cytotoxic, degrades, significantly contracts, causes cancer and leads to an untoward inflammatory response are without support in the reliable scientific literature. While cytotoxicity was noted in an in vitro cell assay presented to the FDA in the 510k of the TVT, the overall clinical data was also presented which did not show cytotoxicity. The clinical data since also do not demonstrate cytotoxicity or an adverse inflammatory effect, as the mesh incorporates, there is long term efficacy and low complications. Moreover, if the mesh was cytotoxic, it would not incorporate and there would be tissue necrosis in all of the patients implanted, which has not been demonstrated.

Degradation of the mesh has not been demonstrated by reliable data. While there have been reports of "surface cracking" (only a few microns) such as that described in the Clave 2010 paper, the authors there confirm that the phenomenon, which was only observable in a minority of specimens, could not be demonstrated on analytical chemical testing. Moreover, the methodology of the paper was flawed and unable to rule out that the surface cracking was not biofilm and/or the effect of surgical removal of the mesh. The data do not support that any surface cracking causes clinical symptoms. To the contrary, polypropylene is a stable and well-accepted biomaterial with a history of over five decades of use in mesh implants. (AUGS SUFU FAQ to Providers 2014; Ford 2015 Cochrane Review) While plaintiffs' experts hypothesize that surface changes lead to

adverse clinical outcomes, this is not supported by the extensive peer-reviewed literature related to polypropylene mesh repairs. As noted in my General TVT report, prospective studies have followed patients with implanted with TVT and TVT-O for 5-17 years and show excellent durability and safety with the use of the macroporous Prolene polypropylene sling. (AUGS-SUFU FAQs by Providers on Mid-urethral Slings for SUI 2014; Tommaselli GA, et al. Medium-term and long-term outcomes following placement of midurethral slings for stress urinary incontinence: a systematic review and metaanalysis. Int Urogynecol J. 2015; 26:1253-68; Ford AA, et al. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database Syst Rev. 2015 Jul 1;7:CD006375. [Epub ahead of print] PubMed PMID: 26130017; Nilsson CG, et al. Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. Int Urogynecol J. 2013; 24:1265-69).

There are no reliable scientific data that show a risk of cancer and reliance by Plaintiff's experts on MSDS sheets and data in rats while attempting to extrapolate to humans is unreliable and improper methodology. (Moalli P, et al. Polypropylene mesh: evidence for lack of carcinogenicity. Int Urogynecol J. 2014; 25:573-6; King AB, Goldman HB. Current controversies regarding oncologic risk associated with polypropylene midurethral slings. Curr Urol Rep. 2014; 15:453.) There are no epidemiologic data which shows that there is a statistically significant risk compared to the background rate of malignancy. King reported a series of 2,361 polypropylene midurethral slings with a follow-up extending up to 122.3 months and the rate of cancer formation was 0.0 % and no sarcomas were reported. (King AB, et al. Is there an association between

polypropylene midurethral slings and malignancy? Urology 2014; 84:789-92). As observed by AUGS and SUFU in their 2014 Frequently Asked Questions by Providers on MUS for SUI:

Tumors related to the implantation of surgical grade polypropylene for mid-urethral slings in humans have never been reported. There is no compelling evidence supporting human malignant transformation related to polypropylene despite the millions of individuals implanted with various forms of this material spanning well over a half century world-wide. The possibility that biomaterial prosthetic devices could cause tumors or promote tumor growth has been the focus of extensive research by both clinicians and biomaterial researchers. (McGregor, D.B., et al., Evaluation of the carcinogenic risks to humans associated with surgical implants and other foreign bodies - a report of an IARC Monographs Programme Meeting. International Agency for Research on Cancer. Eur J Cancer, 2000. 36(3): p. 307-13; Ratner, B.D., et al., eds. Biomaterials Science: An Introduction to Materials in Medicine - 3rd Edition. 2013, Academic Press: Waltham, MA.) It is known that tumor formation related to biomaterials in animals is largely dependent on the physical, not the chemical configuration of the implant, with smooth large surface areas (discs and thin sheets) being potentially carcinogenic, and irregular disrupted surfaces (e.g. those that contain pores as in meshes) lacking carcinogenicity (Ratner, B.D., et al., eds. Biomaterials Science: An Introduction to Materials in Medicine - 3rd Edition. 2013, Academic Press: Waltham, MA.; Oppenheimer, B.S., et al., The latent period in carcinogenesis by plastics in rats and its relation to the presarcomatous stage. Cancer, 1958. 11(1): p. 204-13.).

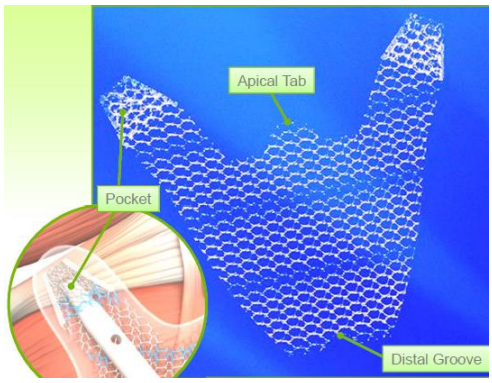
Most recently, a study of 2,474 patients who underwent polypropylene sling placement and followed for a median of 5 years demonstrated that there is no association between polypropylene and cancer or sarcoma in humans. (Linder 2016). Only 2 malignancies (0.08 %) occurred after sling placement while there 49 cancer diagnoses which preexisted the sling placement, demonstrating a much higher background rate of cancer. No cases were seen in patients with more than 10 years follow up. No data have shown a statistically significant higher rate of sarcoma formation or cancer compared to background rates in women.

The Ethicon Gynemesh PS and Prolift IFU, Surgical Technique Guide, Surgeons Resource Monograph and Professional education materials properly identify the steps for using Gynemesh PS and Prolift and adequately and appropriately warn surgeons of the risks associated with the device. The risks of Gynemesh PS and Prolift were appropriately identified in the IFU, were taught in surgeons' education and training, and were widely publicized in peer-reviewed literature, at professional meetings, and in the FDA 2008 and 2011 Public Health Notices. As noted above, these data were presented at conferences and also published in the peer reviewed literature, with peer reviewed papers being furnished to surgeons. Moreover, pain, erosion, scarring, contraction and dyspareunia and many other risks are warned of in the Ethicon IFU, Professional Education materials, Surgeon's Monographs, Patient Counseling materials, Patient Brochures, and other materials and are basic risks pelvic floor surgeons would be expected to know of having gone through medical school, residency and training. Any specific warnings that may be identified by Plaintiff's experts either were not necessary or were adequately included in

the Gynemesh PS and Prolift IFU and accompanying materials mentioned above, as well as in the literature and professional education materials.

D. Prosima

Prosima is a trocar-less pelvic organ prolapse device which utilizes the proven Gynemesh PS mesh combined with anterior and/or posterior inserters and a VSD/balloon device and is indicated for moderate, Stage 2-3 pelvic organ prolapse. The mesh is Y shaped and contains an apical tab and preformed pockets on the implant straps to enable placement with the inserters. The inserters are used to insert the implant straps into dissected tissue channels. The VSD is designed to provide postoperative support for the vaginal tissues after mesh placement and closure of the vaginal incisions. It is trimmed to size. The balloon is designed to replace postsurgical gauze packing and is removed the day after surgery.



Clinical research on the Prosima prototype began in 2004 and continued following FDA 510k clearance in February 2007. Prosima was not broadly launched until later in August 2010 at the joint ICS and IUGA conference in Toronto following additional clinical data.

Carey et al. reported on 95 women implanted with Gynemesh PS mesh and placement of a vaginal support device (VSD) between June 2004 and January 2005 at two centers and were studied prospectively. (Carey 2008) At 12 months, objective success was 85% and subjective success was 87%. Site specific and nature of failures were discussed in the article. Quality of life scores significantly improved at 12 months compared with baseline ($P < 0.0001$). Operative and post-operative complications were discussed. There were 4 (4.2%) mesh exposures with two treated with excision and two treated with estrogen. Sexual dysfunction was reported by 58% of sexually active women preoperatively and 23% at 12 months. It was also reported that sexual dysfunction requiring further surgery was due to a mid-vaginal constriction in three women and a perineal band in one woman (Table 5). Potential benefits and risks including the risk of dyspareunia and mesh exposure of existing techniques and surgeries, as well as the subject device were discussed in the article which was peer reviewed and published for surgeons.

Cadaver studies demonstrated the accurate and safe placement of the Gynemesh PS mesh with Prosima in a cadaver model with and without pelvic organ prolapse. (Reisenauer 2009 IUGA; Reisenauer Am J Obstet Gynecol 2010).

Results of the Ethicon company sponsored Prosima multi-center study were presented at various conferences including IUGA and AUA in 2009. (Slack 2009 IUGA; Zyczynski 2009 AUA). In 2010, the one year anatomic and functional outcomes including complications from this multicenter, international prospective study of 136 patients were published and made available to surgeons. (Zyczynski et al. Am J Obstet Gynecol 2010) Overall in my opinion, the study showed improved anatomic and functional outcomes at 1 year and a low rate of complications and demonstrates that Prosima is safe, effective, and a desirable option for moderate prolapse.

Anatomic success (stage 0-1) was seen in 76.9% of patients and in 86.9% of the cases, the leading vaginal edge was above the hymen. This is where prolapse tends to become symptomatic, and is consistent with the fact that only 14% of patients reported awareness of their prolapse at 1 year, while 91% of the women reported awareness of their prolapse at baseline.

Importance in retention of the VSD for at least 21 days was noted as shortened wear of the VSD was associated with inferior anatomic support at 1 year. Curtailed wear of VSD resulted from it falling out (6 women), removal by the surgeon for suspected vaginal infection (2 women), patient discomfort (2 women), and convenience in scheduling (7 women). Median visual analog scale scores for vaginal support device awareness and discomfort at 3-4 weeks were 2.6 and 1.2, respectively (0=none to 10=worst possible). Pain at 3-4 weeks was also exceptionally low at 0.1 (0=no pain to 10=worst pain imaginable). (Table 2)

Large statistically significant improvements were seen in symptoms and Quality of Life (QoL) scores compared with baseline as recorded by Pelvic Floor Distress Inventory–20 questionnaire (PFDI-20) and the Pelvic Floor Impact Questionnaire–7 (PFIQ-7) which demonstrate positive effect of the device for the patients. (Table 4) All 3 major areas of symptoms (bowel, bladder, and prolapse) were significantly better and translated into QoL improvements. Based on Patient Global Impression of Change (PGI-C), 73.3% of patients indicated that they were "much better" and an additional 15.3% indicated that they were "a little better." (89% of the women reported that their prolapse was "much better" or "a little better" 1 year after surgery).

Complications and complication management were also reported. Mesh exposure occurred in 12 patients (8.0%). Eight exposures resolved after partial mesh excision and 4 exposures were ongoing at 1 year. Most of the exposures were identified before or at the 6-month examinations.

In addition, in my opinion, there was a positive effect on dyspareunia and sexual function in patients treated with Prosima. 9 of 11 women who reported dyspareunia at baseline indicated resolution of dyspareunia at 1 year as compared to 3 reports of de novo dyspareunia. Moreover, twelve women (16.4%) who had not been sexually active at baseline resumed sexual intercourse without new onset dyspareunia. Additionally, statistically significant increases in Pelvic Organ Prolapse/Urinary Incontinence Sexual Function–12 (PISQ-12) scores were reported by sexually active patients (Table 4). These data demonstrate the positive effect of Prosima and show that the device does not cause

an unacceptable risk of pain with intercourse. To the contrary, these data demonstrate the beneficial characteristics of using mesh and the rates and improvements seen are better than native tissue repairs, which are known to lead to de novo dyspareunia. (Francis 1961; Karram 2013) De novo urge and stress urinary incontinence symptoms as reported on the urinary subscale of the PFDI were low and each reported by 4% of the women.

The following year, the medium term (29 month) outcomes of the Prosima study were presented at IUGA and AUGS and published in the peer reviewed literature, which again demonstrated continued efficacy and safety in moderate prolapse. (Sayer IUJ 2011) Anatomic success in this group of 110 patients who consented to follow up was 69.1% and in 84.5% of the cases, the leading vaginal edge was above the hymen. The sustained success rates reported with using the leading edge above the hymen definition (84.5%) were consistent with the patient's report of “much better” on the PGI-C global scale (82.6%, with a further 7.3% reporting their prolapse was “a little better”). When the VSD was retained for at least 21 days anatomic success at ≥2 years was 72.2% and when defined as leading edge above the hymen, it was 87.6%.

Again, large statistically significant improvements from baseline were observed and sustained over time in symptoms and QoL using the PFDI-20 and PFIQ-7 questionnaires. Pelvic symptoms and sexual function improved significantly from baseline ($p<0.01$).

The improvement in mean PISQ-12 scores reported by sexually active patients were statistically significant. Again there was a positive overall effect on dyspareunia. At baseline, dyspareunia was reported in ten sexually active patients (20%). By ≥2 years, seven of these ten women reported resolution of dyspareunia; two were not sexually active due to partner-related reasons and one patient had missing information. Two women who were sexually active at baseline reported de novo dyspareunia symptoms; in one case, the cause of dyspareunia was considered related to vulvodynia, and in the other case, the cause was considered unknown. Additionally, of the 60 non-sexually active women at baseline, 9 reported that they had resumed sexual activity by ≥2 years. Two of these patients reported dyspareunia; in both cases, the cause of dyspareunia was unknown.

In this sub-set of patients from the original study, mesh exposures were reported in 9.1% of patients (11 of 121 patients, consisting of the cohort of 110 patients and an additional 11 device run-in (DRI) cases who returned for extended follow-up which were included in safety analyses). There were 14 episodes of mesh exposure in these 11 patients, which were identified at the following times: four cases at or before 3 months post-procedure; seven at 6 months; one at 8 months post-procedure; one at 1 year; and one at 28 months. The exposed mesh was partially excised in eight patients, two of whom had second excisions. One patient who had a very small (<0.5 cm) exposure identified at 6 months was not given any treatment, and this event was resolved by 1 year. Two patients were treated conservatively with topical estrogen, one of whom required further treatment with topical estrogen when a new mesh exposure was identified at

approximately 28 months. Five percent of patients reported stress urinary incontinence and 3.3% required further prolapse surgery. These data demonstrate the positive effect of Prosima and show that the device does not cause an unacceptable risk of pain with intercourse and that late exposure is uncommon as only one report of mesh exposure occurred beyond 1 year (0.8% at 28 months), which resolved following treatment with topical estrogen.

Additional studies on the Prosima device have shown that it is safe, effective and has a low complication rate. (D'Afiero 2011 IUGA Pres 150; Khandwala 2011 AUGS Poster 143; Krofta 2011 IUGA Pres 116; 2011 Malinowski IUGA Pres 472; Singh 2011 ICS Abstract 575; Chen 2012 Chin J Obstet Gyn; DAfiero 2012 Int J Gynecol Obstet 19S3 Abs 0156; Hung Int Urogynecol J 2012; 23(Suppl 2):S202-203; Bezhenar 2013 - ICS Abs 765; Tsai Taiwan J Obstet Gynecol. 2014; 53(3):337-42). These data show a positive effect on sexual dysfunction and dyspareunia and a rate of mesh exposure that is generally less than 10%.

The largest of these studies, Singh 2011, was conducted in 116 women and at 12 months showed 92.2% anatomic success, significant improvements in patients' quality of life (PFDI-20, $p< 0.001$), and a mesh exposure rate of 2.6%. There was statistically significant improvement in sexual function compared to baseline (PISQ-12, $p= 0.008$). This is consistent with other Prosima data. For example, in the second largest cohort of 94 patients reported by Khandwala, mesh exposure was found in 5.3% (n=5) of patients. 2 resolved after partial excision, 1 resolved with estrogen, and 2 cases ongoing episodes.

Dyspareunia was present at baseline in 8 of 35 (22.9%) sexually active patients and after surgery four of the eight (50%) had resolution. There were two patients (7.4%) who developed de novo dyspareunia out of the 27 who were sexually active without dyspareunia at baseline.

Similarly, Tsai 2014 reported that while baseline dyspareunia was 36.4% (8/22 patients), it dropped to 26.7% (4/15) after treatment with Prosima. Beheznar 2013 reported one case of dyspareunia, but the patient had dyspareunia at baseline. Sexual function by PISQ-12 scores statistically significantly improved. 41.1% of patients resumed sex and 5 patients (8.9%) started sexual intercourse after a long break (about 8 years), without any reported dyspareunia. Anatomic cure was 96% at 12 months. While there was a 14% mesh exposure rate, the patients still demonstrated statistically significant improvements in quality of life. The authors concluded that Prosima demonstrates success, both for anatomical and functional recovery of the pelvic organs, for safety because of the low invasiveness and a small amount of complications, satisfaction of the patients with the results of the treatment connected with the disappearance of the complaints related to violation of defecation, urination, as well as improved quality of life and the resumption of sexual activity. These data demonstrate that Prosima is safe, effective and is not defective.

The Ethicon IFU and Professional education materials properly identify the steps for using the Prosima device. The IFU and Professional Education materials for Prosima adequately and appropriately warns surgeons of the risks associated with the device. The

risks of Prosima were appropriately identified in the IFU, were taught in surgeons' education and training, and were widely publicized in peer-reviewed literature, at professional meetings, and in the FDA 2008 and 2011 Public Health Notices. The Professional Education and Ethicon sponsored Prosima study also identified potential risks and rates of complications. As noted above, these data were presented at conferences and also published in the peer reviewed literature, with peer reviewed papers being furnished to surgeons. Moreover, pain, erosion, scarring, contraction and dyspareunia and many other risks are warned of in the Ethicon IFU, Professional Education materials, Surgeon's Monographs, Patient Counseling materials, Patient Brochures, and other materials. Any specific warnings that may be identified by Plaintiff's experts either were not necessary or were adequately included in the Prosima IFU and accompanying materials mentioned above, as well as in the literature and professional education materials.

I hold all opinions to a reasonable degree of medical certainty and reserve the right to supplement my opinions based on new information and to respond to the depositions of plaintiffs' experts.

Christina Pramudji, M.D.
February 25, 2016